Reducing teratoma risk from transplanted stem cells

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The two most serious obstacles to regenerative medicine therapies are potential immune rejection of transplanted cells and the possibility that such cells could form a type of tumor called teratoma.

CIRM grant recipient and professor of Biology at UC San Diego, Yang Xu, is tackling both of these hurdles. He and his colleagues have recently discovered a method to reduce the ability of embryonic stem cells to form teratoma. The approach involves interfering with the function of a key gene, called Nanog, that is involved in maintaining stem cells. Nanog is one of several genes known as plurpotency factors, which work together to keep cells in their embryonic state.

The paper describing this work, entitled "Phosphorylation stabilizes Nanog by promoting its interaction with Pin1", was published this week in the Proceedings of the National Academies of Science. Xu and colleagues found that by inhibiting Nanog function in stem cells, those cells still formed teratoma, but they were only about one-third the size of tumors that formed by control cells.

Xu was quoted in a press release by UCSD as saying the method is only partially effective because "we are targeting only one pathway" and he speculates that targeting multiple pathways simultaneously might provide a more robust inhibition of teratoma formation.

Some important unanswered questions remain. Would inhibition of any key pluripotency factor, for example Oct3, produce the same effect? Are cells with reduced levels of pluripotency factors still able to give rise to normal differentiated cells of diverse types and in sufficient numbers to be useful for therapies? Could a similar effect be achieved by withdrawing growth factors, such as removing LIF from the media of mouse stem cells or FGF from the media of human stem cells?

Despite these remaining gaps in our understanding, this study provides an exciting foundation for improving the safety of regenerative medicine therapies, any area in the stem field that requires more attention.

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